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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/155,076	10/23/98	GREENFIELD S	263/PPIR2548

HM12/1004

WENDEROTH LIND & PONACK
2033 K STREET N W SUITE 800
WASHINGTON DC 20006

EXAMINER	
TURNER, S	
ART UNIT	**PAPER NUMBER**
1647	12

DATE MAILED: 10/04/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/155,076	Greenfield et al
Examiner	**Group Art Unit**
Sharon L. Turner, Ph.D.	1647

☒ Responsive to communication(s) filed on 8-31-00

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) 13-31 is/are pending in the applicat

Of the above, claim(s) 18-27 is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 13-17 and 28-31 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims 13-31 are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 4

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. The Art Unit of U.S. Patent application SN 09/155,076 has changed. In order to expedite the correlation of papers with the application please direct all future correspondence to Technology Center 1600, Art Unit 1647.

2. The response to the notice to comply with sequence rules filed 1-31-00 has been entered into the record. The preliminary amendment filed 8-31-00 has been entered into the record. The pending claims have been renumbered 13-31 in accordance with applicants request and Rule 1.26.

Election/Restriction

3. Applicant's election of Group I, now renumbered claims 13-17 and 28-31 in Paper No. 7, filed 9-21-99 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

4. Claims 18-27 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 7.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

6. Claims 13-17 and 28-31 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial, credible asserted utility or a well established utility.

Applicants specification p. 3, lines 13-15, 21-23, p. 4, lines 21-24, 29-30 and p. 5, lines 1-4 state hypothetical goals of the invention, i.e., it is expected to find application in specific therapies for combating stroke and other problems of cerebral circulation, antagonists of the non-cholinergic action of AchE are expected to be of interest in the prophylaxis and treatment of cancer, the inventors propose that SEQ ID NO:1 (a peptide portion of AchE) or a related peptide from this region of AchE acts alone or in synergism with a fragment of beta-amyloid to contribute to neuronal degeneration and that the invention provides the peptide containing at least six amino acid residues and having at least 70% homology with part or all of the sequence of SEQ ID NO:1. Based on such disclosure the specification merely sets out research goals to discover the real world use and properties of the disclosed peptides and mixtures.

The specification at page 11-12 discoses the sole effect of enhanced calcium influx into neurons under experimental conditions that do not reflect the in vivo milieu (i.e., magnesium free perfusion). While influx of calcium is thought to contribute to neuronal degeneration in stroke, a peptide which induces such calcium influx would not logically have any application for a treatment or for amelioration of stroke. In contrast, such treatment would be expected to exxacerbate disease as discussed by causing calcium influx and neurodegeneration. The specification fails to teach a specific treatment as disclosed which provides benefit for

combatting stroke or other problems of cerebral circulation. There are no disclosed agonists or antagonists, or disclosed assays for such compounds. Thus, for these reasons the specification fails to teach the artisan how to use the variable peptides and peptide mixtures claimed. Thus, the skilled artisan can not readily discern a specific and substantial, credible or well established utility for the claimed amino acids.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 13-17 and 28-31 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial, credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

In addition to the aforementioned deficiencies with respect to utility, the specification fails to teach the skilled artisan how to make and use the claimed peptides, in particular as it relates to the recitation of peptides which are 70% homologous to the recited SEQ ID NO's, or a portion of the recited SEQ ID NO's. The art recognizes the unpredictability of function as it relates to amino acid structure i.e., peptide function is critically dependent and determined by peptide structure, see in particular Skolnick et al., Trends in Biotech, 18(1):34-39, 2000, abstract, Box 2. Thus, partial peptides sequences and sequences bearing percent homology would not be

expected to function the same as similar peptides. Thus, the skilled artisan cannot make and use the claimed peptides and peptide mixtures without further undue experimentation to identify each peptides use.

9. Claims 13-17 and 28-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The specification discloses SEQ ID NO's: 1-5 which correspond to portions of AchE and β-amyloid precursor protein. These SEQ ID NO's provide written description for the peptides designated in the recited SEQ ID NO. However, the claims are directed to or encompass peptides variants from other species, mutated peptides, and peptides that have a recited degree of homology. None of these peptides or peptide mixtures meet the written description provision of 35 USC 112, first paragraph.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that, "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is for purposes of the 'written description' inquiry, whatever is now claimed." (See Vas-Cath at page 1116.)

With the exception of the peptides of SEQ ID NO's:1-5 of the instant application, the skilled artisan cannot envision the detailed chemical structure of the encompassed amino acids and therefore conception is not achieved until reduction to practice has occurred, regardless of

the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. In the instant case applicants merely provide for the sequences disclosed as SEQ ID Nos:1-5.

Therefore, only SEQ ID NO's:1-5, meet the written description provision of 35 USC 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Claim Objections

10. Claim 29 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 29 does not further limit the recited peptides as the sequences are inherently part of a larger protien having homology with the AchE molecule. The peptides share in common amino acid residues. This objection is made in light of the rejection under 35 USC 112, second paragraph as set forth below.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 14-17 and 28-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The metes and bounds of "comprising or consisting of" (claim 14) is indefinite because one cannot discern whether the claim either consists of or comprises. As the peptides differ accordingly, the metes and bounds of the claim are indeterminate.

Claim 17 is indefinite because it recites "the peptide" which has duplicative antecedent basis as it depends from claim 15, a mixture which further comprises another peptide. The claim should be amended to clearly refer to which peptide of the mixture is labeled or immobilized.

Claim 29 is indefinite as it is unclear what further limitation applicants wish to recite. The examiner notes that all amino acids are related via homology as they commonly share amino acid residues.

Claim Rejections - 35 USC § 102 or 103

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 13-17 are rejected under 35 U.S.C. 102(b) as being anticipated by de Serres et al., Cellular and Molecular Neurobiology, 13(3):279-87, June 1993.

Claims 13-14 are not limited in length because the homolgoy limitaion merely requires that "a part" have 70% homology. Thus, the full length peptide shares 100% homology over that "part" which is SEQ ID Nos:1 and 3-5. Further, the peptides merely require 70% homology and not identity to SEQ ID Nos 1-5. de Serres et al., teach a mixture of peptides including isolated AchE, see in particular p. 282, lines 10-12, crude Ee-AChE, purified Ee-AChE and Bu-ChE, purchased from Wortington Biochemicals, and beta-amyloid precursor protein, see in particular peptide substrates, p. 281, lines 5-6. Thus, the mixture of de Serres constitutes applicants claimed mixture. The AChE peptides are immobilized on a solid support as analyzed by PAB affinity chromatography, see in particular p. 284, last paragraph and Table I, including legend. The amyloid peptides are labeled with both N-[ethyl-2-^{3}H]maleimide and N-ethylmaleimide.

15. Claims 13-14 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Moran et al., Acta Neuropathol., 85:362-369, 1993.

Claims 13-14 are not limited in length because the homolgoy limitaion merely requires that "a part" have 70% homology. Thus, the full length peptide shares 100% homology over that "part" which is SEQ ID Nos:1 and 3-5. Further, the peptides merely require 70% homology and not identity to SEQ ID Nos 1-5. Moran et al., teach colocalization of AchE with a β-amyloid peptide identified by immunocytochemistry using a monoclonal antibody 4G8 (IgG 2b) raised against a synthetic peptide corresponding to amino acids 1-24 of Aβ peptide and labeled with the biotin-extravidin-phosphatase alkaline method. The AchE peptides are labeled, see in particular Cholinesterase histochemistry, p. 363, column 1, lines 26-38 and β-protein

immunocytochemistry, lines 42-column 2, line 2. The beta-amyloid peptide detected constitutes Aβ which shares residues 1-16 of SEQ ID NO:2. Thus, the reference teachings anticipate the claimed invention.

Status of Claims

16. No claims are allowed.

17. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Friday from 7:30 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Sharon L. Turner, Ph.D.
October 1, 2000

Patricia A. Duffy

PATRICIA A. DUFFY
PRIMARY EXAMINER